Two Adjustment Methods to Reduce Machine Bias in the Measurement of Hemoglobin Concentration by Portable Hemoglobinometers

Denish Moorthy,[1] Laura Hackl,[1,2] Veronica Varela,[1] Crystal Karakochuk,[3] Dora Inés Mazariegos,[4] Kidola Jeremiah,[5] Omar Obeid,[6] Nirmal Ravi,[7] Desalegn A Ayana,[8] Silvia Alayón,[1] Omar Dary[9]

1. USAID Advancing Nutrition, Arlington, VA, United States; 2. Nestle R&D Nutrition, Lausanne, Switzerland; 3. University of British Columbia, Vancouver, Canada; 4. Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala; 5. National Institute of Medical Research, Mwanza, Tanzania; 6. American University of Beirut, Beirut, Lebanon; 7. eHealth Africa, Abuja, Nigeria; 8. Haramaya University, Dire Dawa, Ethiopia; 9. USAID, Washington, D.C., United States

KEY TAKE-AWAY

Adjustments for systematic bias in hemoglobinometers might be performed using a Bland-Altman mean difference estimation with venous blood hemoglobin measurements.

BACKGROUND

Diagnostic laboratories determine hemoglobin (Hb) spectrophotometrically from venous blood specimens measured in an autoanalyzer (AA). Systematic errors in Hb measurement are mainly a result of device bias, and they may vary from machine to machine. Systematic errors affect the accuracy of Hb measurement, which is critical for making a correct diagnosis of anemia at the individual level, and therefore an accurate estimation of anemia prevalence at the population level. Accuracy is measured by the mean difference of Hb concentration in venous blood samples between a HemoCue® (HC) Hb device and an AA.

METHODS

We compared the accuracy of Hb measurements in venous blood between three HC Hb models (201+, 301, and 801) and an AA in a combined population of 15–49-year-old women of reproductive age (WRA) and 12–59-month-old young children (YC) to cover the range of 50–180 mg/L Hb. We used the Hb data from the Hemoglobin Measurement study, conducted in laboratory settings in Cambodia, Ethiopia, Guatemala, Lebanon, Nigeria, and Tanzania. We used two methods to adjust for device bias: regression calibration and mean-difference correction.

To adjust Hb values using the regression calibration method:

1. **Remove outliers**: We conducted a Bland-Altman analysis and excluded cases for which the difference between AA and HemoCue values were outside the 98 percent limits of agreement (LOA).
2. **Calculate regression parameters**: We regressed AA:Venous (x-axis) vs HC:Venous (y-axis) to calculate intercept (α) and slope (β) for each HemoCue model (201+, 301, and 801).
3. **Use all experimental data to calculate adjusted HC Hb values**: We used the regression results to adjust all values for HC Hb, using the following equation: HC:Venous_adjusted = [HC:Venous - α]/ β.

To adjust Hb values using the mean-difference correction:

1. **Remove outliers:** We conducted a Bland-Altman analysis and excluded cases for which the difference between AA and HemoCue values were outside the 98 percent LOA.
2. **Calculate mean difference*:** We repeated the Bland-Altman analysis on the reduced dataset to estimate the mean difference in Hb concentration between the HC and AA for each model of the HC Hb device in each site. using the following equation: Bland-Altman mean difference = (HC Hb-AA Hb).
3. **Use all experimental data to calculate adjusted HC Hb values:** We adjusted all values for HC Hb using the following equation: HC:Venous_adjusted = [HC + Bland-Altman mean difference].

**This value may be negative if the HC Hb is lower than the AA Hb.*

RESULTS

Both regression calibration and Bland-Altman adjustment improved the accuracy of Hb measures and reduced bias on HemoCue machines equally (table 1). The range of device bias (unadjusted Hb values) across the six sites for the HC Hb 201+ (-2.6–3.8 g/L), 301 (2.4–7.3 g/L), and 801 (2.1–5.9 g/L) was reduced to less than 2 g/L for the 201+ and less than 1 g/L for 301 and 801 device models with one exception.

Table 1. Device Bias and Mean Bias after Adjustments of HemoCue® Hb Devices for Hb Measurement from Venous Blood in Combined Populations of WRA and YC

HemoCue® Hb Model	Study Site	Device Bias Before Adjustment (Hb, g/L)	Bias After Adjustment (Hb, g/L)	
			Regression	Mean Difference
201+	Guatemala	-1·7	-0·2	-0·2
	Cambodia	-1·0	0·2	0·2
	Tanzania	3·8	-0·6	-0·6
	Lebanon	-1·0	-0·6	-0·6
	Ethiopia	3·4	0·0	0·0
	Nigeria	-2·6	-1·7	-1·6
301	Guatemala	1·9	-0·1	-0·1
	Cambodia	7·3	0·2	0·2
	Tanzania	6·2	-0·6	-0·6
	Lebanon	6·5	-0·8	-0·8
	Ethiopia	2·4	0·2	0·2
	Nigeria	4·5	-0·3	-0·3
801	Guatemala	2·1	-0·5	-0·5
	Cambodia	2·7	0·0	0·0
	Lebanon	3·0	-0·9	-0·8
	Ethiopia	5·9	0·7	0·7

CONCLUSIONS

In almost all cases, we found that adjustment for device bias using either regression calibration or mean-difference correction reduced the bias to less than 1 g/L, which is an excellent benchmark. While the mean-difference adjustment is an easier method to conduct, we considered both methods, because the key assumption for using the mean-difference method—that systematic bias is constant across the range of Hb concentrations (i.e., slope near 1.0)—may not always be met. We recommend that users of the HC should estimate the mean-difference adjustment method to reduce machine bias and standardize all devices to a systematic error lower than 1.0 g/L.

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